

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 March 2001 (15.03.2001)

PCT

(10) International Publication Number
WO 01/18016 A1

- (51) International Patent Classification⁷: **C07H 21/02**
- (21) International Application Number: **PCT/US00/18174**
- (22) International Filing Date: **30 June 2000 (30.06.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
09/393,996 **10 September 1999 (10.09.1999)** **US**
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- (81) Designated States (*national*): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.**
- (84) Designated States (*regional*): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**
- Published:**
— *With international search report.*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **NOVEL GENES ENCODING PROTEINS HAVING PROGNOSTIC, DIAGNOSTIC, PREVENTIVE, THERAPEUTIC, AND OTHER USES**

(57) Abstract: The invention provides isolated nucleic acids encoding a variety of proteins having diagnostic, preventive, therapeutic, and other uses. These nucleic acid and proteins are useful for diagnosis, prevention, and therapy of a number of human and other animal disorders. The invention also provides antisense nucleic acid molecules, expression vectors containing the nucleic acid molecules of the invention, host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a nucleic acid molecule of the invention has been introduced or disrupted. The invention still further provides isolated polypeptides, fusion polypeptides, antigenic peptides and antibodies. Diagnostic, screening, and therapeutic methods utilizing compositions of the invention are also provided. The nucleic acids and polypeptides of the present invention are useful as modulating agents in regulating a variety of cellular processes.

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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule having a nucleotide sequence which is at least 40% identical to the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 5 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

b) a nucleic acid molecule comprising at least 15 nucleotide residues and having a nucleotide sequence identical to at least 15 consecutive nucleotide residues of any of SEQ ID 10 NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

c) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, 15 and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

d) a nucleic acid molecule which encodes a polypeptide having an amino acid sequence comprising at least 8 consecutive amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence 20 encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438; and

e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, wherein the nucleic acid molecule 25 hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

5 a) a nucleic acid having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof; and

10 b) a nucleic acid molecule which encodes a polypeptide having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

3. The nucleic acid molecule of claim 1, further comprising vector nucleic acid sequences.

15 4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous polypeptide.

5. A host cell which contains the nucleic acid molecule of claim 1.

20 6. The host cell of claim 5 which is a mammalian host cell.

7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

25 8. An isolated polypeptide selected from the group consisting of:

a) a fragment of a polypeptide having an amino acid sequence comprising at least 8 contiguous amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-

76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438;

b) a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions; and

c) a polypeptide which is encoded by a nucleic acid molecule having a nucleotide sequence which is at least 40% identical to any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32, 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

9. The isolated polypeptide of claim 8, having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof.

10. The polypeptide of claim 8, wherein the amino acid sequence of the polypeptide further comprises heterologous amino acid residues.

11. An antibody which selectively binds with the polypeptide of claim 8.

12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide having the amino acid sequence of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof;

5 b) a polypeptide having an amino acid sequence which comprises at least 8 contiguous amino acid residues of any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438; and

10 c) a naturally occurring allelic variant of a polypeptide having an amino acid sequence comprising any of SEQ ID NOs: 3-5, 13-15, 23-28, 33-38, 43-54, 63-76, 83-92, 93, 103-105, and 123, or the amino acid sequence encoded by a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes with a nucleic acid molecule having the nucleotide sequence of any of SEQ ID NOs: 1, 2, 11, 12, 21, 22, 31, 32,
15 41, 42, 61, 62, 81, 82, 91, 92, 101, 102, 121, and 122, the nucleotide sequence of a cDNA clone deposited with ATCC® as any of Accession Nos. PTA-424, PTA-425, and PTA-438, or a complement thereof under stringent conditions;

the method comprising culturing the host cell of claim 5 under conditions in which the nucleic acid molecule is expressed.

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13. A method for detecting the presence of a polypeptide of claim 8 in a sample, comprising:

a) contacting the sample with a compound which selectively binds with a polypeptide of claim 8; and

25 b) determining whether the compound binds with the polypeptide in the sample.

14. The method of claim 13, wherein the compound which binds with the polypeptide is an antibody.

15. A kit comprising a compound which selectively binds with a polypeptide of claim 8 and instructions for use.

16. A method for detecting the presence of a nucleic acid molecule of claim 1 in a sample, comprising the steps of:

- a) contacting the sample with a nucleic acid probe or primer which selectively hybridizes with the nucleic acid molecule; and
- b) determining whether the nucleic acid probe or primer binds with a nucleic acid molecule in the sample.

17. The method of claim 16, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

18. A kit comprising a compound which selectively hybridizes with a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which binds with a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- b) determining whether the polypeptide binds with the test compound.

20. The method of claim 19, wherein the binding of the test compound with the polypeptide is detected by a method selected from the group consisting of:

- a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay;
- c) detection of binding using an assay for an activity characteristic of the polypeptide.

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds with the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

a) contacting a polypeptide of claim 8 with a test compound; and

b) determining the effect of the test compound on the activity of the polypeptide to
10 thereby identify a compound which modulates the activity of the polypeptide.

23. An antibody substance which selectively binds with the polypeptide of claim 8, wherein the antibody substance is made by providing the polypeptide to an immunocompetent vertebrate and thereafter harvesting blood or serum from the vertebrate.

Fig. 1A

I S K G I A D I I M I A F R T R V H G R C 168
 ATT TCA AAG GGG ATT GCA GAC ATC ATG ATT GCC TTT AGG ACT CGA GTC CAT GGT CGG TGT 548

 P R Y F D G G P L G V L G H A F P P G P G 188
 CCT CGC TAT TTT GAT GGT CCC TTG GGA GTG CTT GGC CAT GCC TTT CCT CCT GGT CCG GGT 608

 L G G D T H F D E D E N W T K D G A G F 208
 CTG GGT GGT GAC ACT CAT TTT GAT GAG GAT GAA AAC TGG ACC AAG GAT GGA GCA GGA TTC 668

 N L F L V A A H E F G H A L G L S H S N 228
 AAC TTG TTT CTT GTG GCT GCT CAT GAA TTT GGT CAT GCA CTG GGG CTC TCT CAC TCC AAT 728

 D Q T A L M F P N Y V S L D P R K Y P L 248
 GAT CAA ACA GCC TTG ATG TTC CCA AAT TAT GTC TCC CTG GAT CCC AGA AAA TAC CCA CTT 788

 S Q D D I N G I Q S I Y G G L P K V P A 268
 TCT CAG GAT GAT ATC AAT GGA ATC CAG TCC ATC TAT GGA GGT CTG CCT AAG GTA CCT GCT 848

 K P K E P T I P H A C D P D L T F D A I 288
 AAG CCA AAG GAA CCC ACT ATA CCC CAT GCC TGT GAC CCT GAC TTG ACT TTT GAC GCT ATC 908

 T T F R R E V M F F K G R H L W R I Y Y 308
 ACA ACT TTC CGC AGA GAA GTA ATG TTC TTT AAA GGC AGG CAC CTA TGG AGG ATC TAT TAT 968

Fig. 1B

D	I	T	D	V	E	F	E	L	I	A	S	F	W	P	S	L	P	A	D	328
GAT	ATC	ACG	GAT	GTT	GAG	TTT	GAA	TTA	ATT	GCT	TCA	TTC	TGG	CCA	TCT	CTG	CCA	GCT	GAT	1028
L	Q	A	A	Y	E	N	P	R	D	K	I	L	V	F	K	D	E	N	F	348
CTG	CAA	GCT	GCA	TAC	GAG	AAC	CCC	AGA	GAT	AAG	ATT	CTG	GTT	TTT	AAA	GAT	GAA	AAC	TTC	1088
W	M	I	R	G	Y	A	V	L	P	D	Y	P	K	S	I	H	T	L	G	368
TGG	ATG	ATC	AGA	GGA	TAT	GCT	GTC	TTG	CCA	GAT	TAT	CCC	AAA	TCC	ATC	CAT	ACA	TTA	GGT	1148
F	P	G	R	V	K	K	I	D	A	A	V	C	D	K	T	T	R	K	T	388
TTT	CCA	GGA	CGT	GTG	AAG	AAA	ATA	GAT	GCA	GCC	GTC	TGT	GAT	AAG	ACC	ACA	AGA	AAA	ACC	1208
Y	F	F	V	G	I	W	C	W	R	F	D	E	M	T	Q	T	M	D	K	408
TAC	TTC	TTT	GTG	GGC	ATT	TGG	TGC	TGG	AGG	TTT	GAT	GAA	ATG	ACC	CAA	ACC	ATG	GAC	AAA	1268
G	F	P	Q	R	V	V	K	H	F	P	G	I	S	I	R	V	D	A	A	428
GGA	TTC	CCG	CAG	AGA	GTG	GTA	AAA	CAC	TTT	CCT	GGA	ATC	AGT	ATC	CGT	GTT	GAT	GCT	GCT	1328
F	Q	Y	K	G	F	F	F	F	S	R	G	S	K	Q	F	E	Y	N	I	448
TTC	CAG	TAC	AAA	GGA	TTC	TTC	TTT	TTT	AGC	CGT	GGA	TCA	AAG	CAA	TTT	GAA	TAC	AAC	ATT	1388
K	T	K	N	I	T	R	I	M	R	T	N	T	W	F	Q	C	K	E	P	468
AAG	ACA	AAG	AAT	ATT	ACC	CGA	ATC	ATG	AGA	ACT	AAT	ACT	TGG	TTT	CAA	TGC	AAA	GAA	CCA	1448

Fig. 1C

K	N	S	S	F	G	F	D	I	N	K	E	K	A	H	S	G	G	I	K	488
AAG	AAC	TCC	TCA	TTT	GGT	TTT	GAT	ATC	AAC	AAG	GAA	AAA	GCA	CAT	TCA	GGA	GGC	ATA	AAG	1508
I	L	Y	H	K	S	L	S	L	F	I	F	G	I	V	H	L	L	K	N	508
ATA	TTG	TAT	CAT	AAG	AGT	TTA	AGC	TTG	TTT	ATT	TTT	GGT	ATT	GTT	CAT	TTG	CTG	AAA	AAC	1568
T	S	I	Y	Q	*															514
ACT	TCT	ATT	TAT	CAA	TAA															1586
ATT	CAT	AGAC	CTAA	AAATA	AAACCT	CAAC	AGG	CTTTT	TAATA	TAAATT	CTGCTT	CAAAA	TAGAA	TAA	AAACCAT	TCTTT	TAAC			1665
AAC	AAAA	AAAA	AAAA	AAAA	AAAA	AAAA														1684

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Fig. 1D